

**U.S.S.N. 09/482,682**  
**VON SEGGERN *et al.***  
**AMENDMENT AFTER FINAL**

**IN THE CLAIMS:**

A listing of the claims, in accord with 37 CFR §1.121, is provided. The listing of claims replaces all prior such listings of claims. Claims 1, 2, 6, 9, 12, 14, 18, 41, 47, 95-97 and 100 are amended herein. Claim 13 is cancelled herein.

1. (Currently Amended) An isolated nucleic acid molecule comprising: a sequence of nucleotides encoding an adenovirus tripartite leader (TPL), wherein the TPL-encoding sequence of nucleotides comprises: (a) first and second different TPL exons, wherein the different TPL exons are from different adenoviruses, or in a non-native order or both or (b) first, second and third same or different TPL exons, wherein:

at least two of the different TPL exons are from different adenoviruses, or in a non-native order or both; and

said TPL exons in (a) and (b) are selected from the group consisting of complete TPL exon 1, complete TPL exon 2 and complete TPL exon 3.

2. (Currently Amended) An isolated nucleic acid molecule, comprising: a sequence of nucleotides encoding an adenovirus tripartite leader (TPL) that comprises (a) first and second different TPL exons, wherein the different TPL exons are from different adenoviruses, or in a non-native order or both or (b) first, second and third same or different TPL exons, wherein at least two of the different TPL exons are from different adenoviruses, or in a non-native order or both, said TPL exons in (a) and (b) selected from the group consisting of complete TPL exon 1, partial TPL exon 1, complete TPL exon 2 and complete TPL exon 3, wherein the sequence of nucleotides encoding a TPL is operatively linked to an intron containing an RNA processing signal.

3. (Cancelled)

4. (Previously Presented) The isolated nucleic acid molecule of claim 2, wherein said intron is native adenovirus intron 1.

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5. (Previously Presented) An isolated nucleic acid molecule, comprising a sequence of nucleotides encoding an adenovirus tripartite leader (TPL), wherein said TPL nucleotide sequence is set forth in SEQ ID NO: 32.

6. (Currently Amended) An isolated nucleic acid molecule, comprising an adenovirus tripartite leader (TPL) nucleotide sequence, said TPL nucleotide sequence comprising (a) first and second different TPL exons, wherein the different TPL exons are from different adenoviruses, or in a non-native order or both or (b) first, second and third same or different TPL exons, wherein at least two of the different TPL exons are from different adenoviruses, or in a non-native order or both, said TPL exons in (a) and (b) selected from the group consisting of complete TPL exon 1, partial TPL exon 1, complete TPL exon 2 and complete TPL exon 3 and further comprising a promoter and a sequence of nucleotides that encodes an adenoviral structural protein, operatively linked to said promoter and said TPL-encoding sequence of nucleotides.

7. (Previously Presented) The isolated nucleic acid molecule of claim 6, wherein said adenoviral structural protein is a fiber protein or a chimeric protein which includes an adenovirus fiber protein tail domain.

8. (Previously Presented) The isolated nucleic acid molecule of claim 7, wherein said chimeric protein comprises an Ad3 head domain and an Ad5 tail domain or an Ad5 head domain and an Ad3 tail domain.

9. (Currently Amended) [[The]]An isolated nucleic acid molecule of claim 7, wherein comprising a sequence of nucleotides encoding an adenovirus tripartite leader (TPL), wherein the TPL-encoding sequence of nucleotides comprises first, second and third TPL exons selected from the group consisting of complete TPL exon 1, partial TPL exon 1, complete TPL exon 2 and complete TPL exon 3, wherein:

the sequence of nucleotides encoding the TPL is operatively linked to an intron containing an RNA processing signal;

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said molecule further comprises a promoter and a sequence of nucleotides that encodes an adenovirus fiber protein or a chimeric protein which includes an adenovirus fiber protein tail domain operatively linked to said promoter and said TPL-encoding sequence of nucleotides; and

    said molecule is contained in a plasmid selected from the group consisting of plasmids pDV60, pDV67, pDV69, pDV80 and pDV90.

10. (Previously Presented) The isolated nucleic acid molecule of claim 9, wherein said molecule has a nucleotide sequence selected from the group consisting of sequences shown in SEQ ID NO: 43, SEQ ID NO: 44, SEQ ID NO: 47, SEQ ID NO: 64 and SEQ ID NO: 65.

11. (Original) An adenovirus vector complementing plasmid comprising an isolated nucleic acid molecule according to claim 1.

12. (Currently Amended) An adenovirus vector packaging cell line, comprising:

    i) a stably integrated nucleic acid molecule, comprising an adenovirus tripartite leader (TPL) nucleotide sequence, said TPL sequence comprising (a) first and second different TPL exons, wherein the different TPL exons are from different adenoviruses, or in a non-native order or both; or (b) first, second and third same or different TPL exons, wherein at least two of the different TPL exons are from different adenoviruses, or in a non-native order or both, said TPL exons in (a) and (b) selected from the group consisting of complete TPL exon 1, partial TPL exon 1, complete TPL exon 2 and complete TPL exon 3; and

    ii) an operatively-linked promoter and a nucleic acid sequence that encodes an adenovirus structural protein,

    wherein the sequence of nucleotides that encodes the TPL ~~consists~~ essentially of comprises a first TPL exon operatively linked to a complete second TPL exon operatively linked to a complete third TPL exon.

13. (Cancelled)

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14. (Currently Amended) An adenovirus vector packaging cell line, comprising:

i) a stably integrated nucleic acid molecule, comprising an adenovirus tripartite leader (TPL) nucleotide sequence, said TPL sequence comprising ~~The cell line of claim 13, wherein said TPL molecule comprises~~ complete TPL exon 1 having the nucleotide sequence of SEQ ID NO: 32 or partial TPL exon 1 having the nucleotide of SEQ ID NO: 26[.] ; and

ii) an operatively-linked promoter and a nucleic acid sequence that encodes an adenovirus structural protein,

wherein the sequence of nucleotides that encodes the TPL comprises a first TPL exon operatively linked to a complete second TPL exon operatively linked to a complete third TPL exon.

15. (Original) The cell line of claim 12 wherein said promoter is an inducible promoter.

16. (Previously Presented) The cell line of claim 12, wherein said adenovirus structural protein is adenovirus fiber protein or a chimeric protein which includes an adenovirus fiber protein tail domain.

17. (Previously Presented) The cell line of claim 16, wherein said chimeric protein comprises an Ad3 head domain and an Ad5 tail domain or an Ad5 head domain and an Ad3 tail domain.

18. (Currently Amended) The cell line of claim [[12]] 14, wherein said nucleic acid molecule is selected from the group consisting of plasmids pDV60, pDV67, pDV69, pDV80 and pDV90.

19. (Previously Presented) The cell line of claim 18, wherein said nucleic acid molecule has a nucleotide sequence selected from the group consisting of sequences shown in SEQ ID NO: 43, SEQ ID NO: 44 and SEQ ID NO: 47.

20. (Previously Presented) The cell line of claim 12, wherein said cell line is an epithelial cell line.

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21. (Previously Presented) The cell line of claim 12, wherein said cell line supports the production of a recombinant adenovirus vector genome by complementation of a deficient viral gene in said vector genome.

22. (Previously Presented) The cell line of claim 21, wherein said cell line expresses an adenovirus early protein gene and a fiber gene.

23. (Previously Presented) The cell line of claim 21, wherein deletion of a deficient viral gene is complemented by the expression of a gene under the control of an inducible promoter.

Claims 24-40 (Cancelled)

41. (Currently Amended) ~~A method for producing an adenovirus particle comprising:~~

1) ~~providing a packaging cell line wherein said packaging cell line comprises:~~

a) ~~a The method of claim 95, wherein said stably integrated first nucleic acid molecule is operatively linked to a promoter, and said first nucleic acid is operatively linked to a second nucleic acid molecule encoding an adenovirus structural protein, wherein said first nucleic acid molecule comprises an adenovirus tripartite leader (TPL) nucleotide sequence operatively linked to an intron containing an RNA processing signal, said TPL nucleotide sequence comprising (a) first and second different TPL exons or (b) first, second and third different TPL exons, said TPL exons selected from the group consisting of complete TPL exon 1, partial TPL exon 1, complete TPL exon 2 and complete TPL exon 3 and~~

b) ~~said cell line supports the production of a recombinant adenovirus vector genome by complementation of a deficient viral gene in said vector genome, and~~

2) ~~producing said adenovirus particle.~~

Claims 42-46 (Cancelled)

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47. (Currently Amended) The method of claim [[41]] 95, wherein the adenovirus structural protein is adenovirus fiber protein.

Claims 48-68 (Cancelled)

69. (Previously Presented) The packaging cell line of claim 12, wherein said cell line is selected from the group consisting of 293, A549, W163, HeLa, Vero, 211, 211A and an epithelial cell line, wherein said cell line comprises said stably integrated nucleic acid molecule.

Claims 70-94 (Cancelled)

95. (Currently Amended) A method for producing an adenovirus particle comprising:

1) providing a packaging cell line wherein said packaging cell line comprises:

[[a]] (i) a stably integrated first nucleic acid molecule operatively linked to a second nucleic acid molecule encoding an adenovirus structural protein, wherein said first nucleic acid molecule comprises the nucleic acid molecule of claim 2; an adenovirus tripartite leader (TPL) nucleotide sequence operatively linked to an intron containing an RNA processing signal, said TPL nucleotide sequence comprising (a) first and second different TPL exons, or (b) first, second and third different TPL exons, said TPL exons selected from the group consisting of complete TPL exon 1, partial TPL exon 1, complete TPL exon 2 and complete TPL exon 3 and

[[b]] (ii) said cell line supports the production of a recombinant adenovirus vector genome by complementation of a deficient viral gene in said vector genome, and

2) producing said virus particle.

96. (Currently Amended) A method for producing an adenovirus particle comprising:

1) providing a packaging cell line wherein said packaging cell line comprises:

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[[a]] (i) a stably integrated nucleic acid molecule, comprising:  
a sequence of nucleotides encoding an adenovirus tripartite leader (TPL), wherein the TPL-encoding sequence of nucleotides comprises: (a) first and second different TPL exons, wherein the different TPL exons are from different adenoviruses, or in a non-native order or both or (b) first, second and third same or different TPL exons, wherein at least two of the different TPL exons are from different adenoviruses, or in a non-native order or both and said TPL exons in (a) and (b) are selected from the group consisting of complete TPL exon 1, complete TPL exon 2 and complete TPL exon 3; and

[[b]] (ii) said cell line supports the production of a recombinant adenovirus vector genome by complementation of a deficient viral gene in said vector genome; and

2) producing said adenovirus particle.

97. (Currently Amended) A method for producing an adenovirus particle comprising:

1) providing a packaging cell line wherein said packaging cell line comprises: a stably integrated nucleic acid molecule, comprising:  
(i) a sequence of nucleotides encoding an adenovirus tripartite leader (TPL), wherein the TPL-encoding sequence of nucleotides comprises: (a) first and second different TPL exons, wherein the different TPL exons are from different adenoviruses, or in a non-native order or both or (b) first, second and third same or different TPL exons, wherein at least two of the different TPL exons are from different adenoviruses, or in a non-native order or both and said TPL exons are selected from the group consisting of complete TPL exon 1, complete TPL exon 2 and complete TPL exon 3, and

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(ii) a sequence of nucleotides encoding adenovirus fiber protein;  
and

2) producing an adenovirus particle.

98. (Previously Presented) The method of claim 97, wherein said adenovirus particle comprises a genome encoding an exogenous protein.

99. (Previously Presented) The method of claim 98, wherein said exogenous protein is selected from a group consisting of a tumor-suppressor protein, a biologically active fragment thereof that has tumor-suppressor activity, a suicide protein and a biologically active fragment thereof that has activity as a suicide protein.

100. (Currently Amended) ~~[[The]]~~An isolated nucleic acid molecule of ~~claim 7 comprising a sequence of nucleotides encoding an adenovirus tripartite leader (TPL), wherein the TPL-encoding sequence of nucleotides comprises first, second and third TPL exons selected from the group consisting of complete TPL exon 1, partial TPL exon 1, complete TPL exon 2 and complete TPL exon 3,~~ wherein:

said molecule further comprises a promoter and a sequence of nucleotides that encodes an adenovirus fiber protein or a chimeric protein which includes an adenovirus fiber protein tail domain operatively linked to said promoter and said TPL-encoding sequence of nucleotides; and

said molecule is contained in plasmid pCLF.

101. (Previously Presented) The isolated nucleic acid molecule of claim 100 that has the sequence of nucleotides set forth in SEQ ID No. 8.

102. (Previously Presented) A plasmid having all of the identifying characteristics of a plasmid deposited at the ATCC under accession no. 97737.

103. (Previously Presented) A plasmid having all of the identifying characteristics of a plasmid deposited at the ATCC under accession no. PTA-1144, PTA-1145, PTA-1146, PTA-1147 or PTA-1148.